# Are Large Volume and On-Body Injectors Ready to Deliver?

**Advances in drug delivery and formulation technologies, coupled with greater awareness of the needs of stakeholders, suggest that these devices are gaining traction in the market. However, there are still challenges to overcome**

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Despite considerable investment in technology development, the market for wearable drug delivery devices for subcutaneous (SC) administration has been in a fledgling state for several years. Outside insulin, only a very small number of On-Body Injector (OBI) devices are marketed or approved for imminent launch.

However, as both drug delivery and drug formulation technologies progress, and the push towards self-administration continues, there are indications that more widespread uptake of On-Body Delivery Systems (OBDS) may finally be on the horizon.

**Biologics and Wearables**

Until recently, the SC delivery of biologics was restricted to drugs that could be self-administered (e.g., away from a clinical setting) using prefilled syringes or autoinjectors, and with volumes in the 1ml to 2ml range. This is a buoyant market space for drug delivery devices of this nature and a small number of respected, well-established devices dominate. Formulation teams frequently target lower volumes to fit such devices where possible, which are well-suited for self-administration and generally accepted by patients.

There is a current trend towards reducing the frequency of dosing, resulting in new biologic drugs for SC injections containing larger concentrations of active ingredients. However, this increases viscosity, resulting in larger delivery volumes to balance the need for a product that can be injected without damage to the molecules or unnecessary patient discomfort. Consequently, it is likely that more SC drugs with volumes of 3ml, 4ml, or even 5ml and beyond, will begin to appear.

Not long ago, 2ml to 5ml dosing was an ideal target for OBI device developers, representing the key battleground for competing devices to secure. Now, though, that has all changed. The first examples of autoinjectors capable of delivering up to 2.25ml of liquid are already commercially available and delivering doses to patients. Further, it is feasible for patients to self-administer consecutive doses via autoinjectors (provided sufficient training and instructions are in place). Despite this, questions remain over the practicalities, including patient comfort.

More recently, two of the leading device manufacturers have launched 5.0ml and 5.5ml autoinjectors using standard primary containers. This is likely to result in plenty of patient-centric data in the coming months to show that it is possible to hold devices with a larger payload comfortably against the skin whilst administration takes place.

The upshot of this is that, while there is a drive towards less frequent dosing, the resultant payloads are increasing in volume. This creates an opportunity for OBI devices, but one that is being eroded by ever-larger autoinjectors.

**IV to SC Switching**

As for immuno-oncology, there is a range of drug products that are typically 10ml volume or more and given to patients intravenously. Although this is effective from a bioavailability and susceptibility viewpoint, it requires an infusion system, syringe pump or

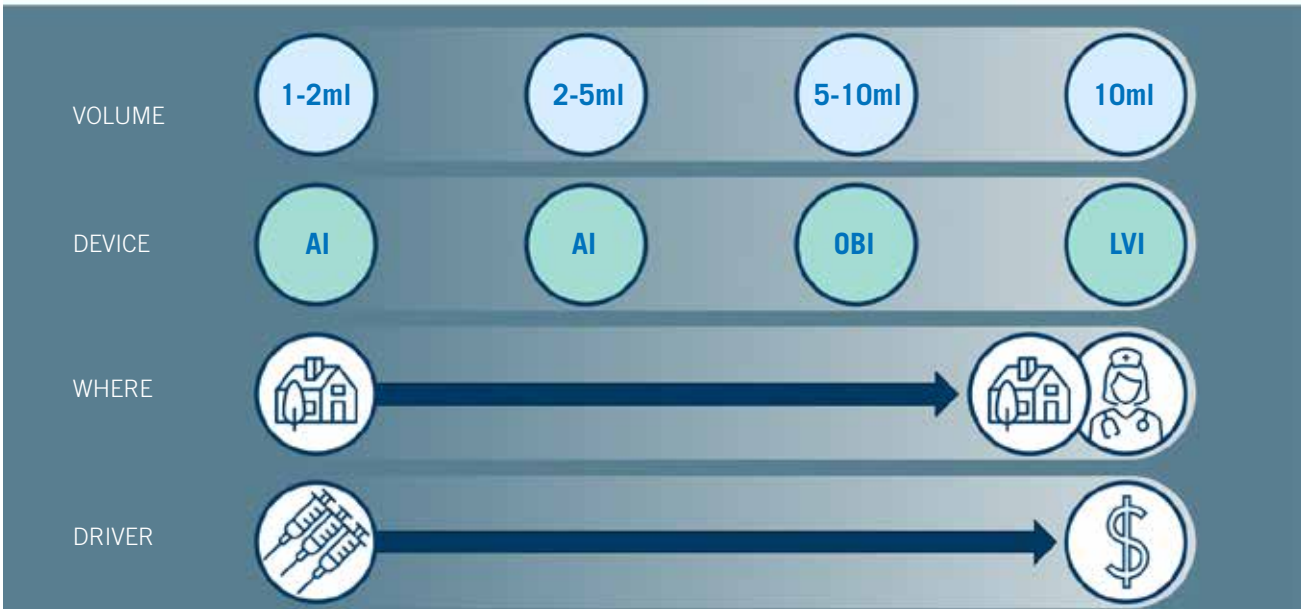


Figure 1. Self-administered SC delivery devices that can deliver across a range of volumes will be in demand.

a hand-held syringe, plus hands-on involvement from a healthcare professional (HCP). This is inconvenient for patients, as it means travel to a clinic and administering the drug can take hours, rather than minutes.

This is a different modality to that of biologics, and there is an emerging trend of marketed intravenously-administered immuno-oncology drugs 'switching' and being reformulated for SC delivery.

Hypothetically, this is a strong catalyst for the OBI market. Volumes are likely to be much higher than any autoinjector or prefilled syringe can accommodate. Two examples on the market include: Roche MabThera SC, delivered as a fixed dose of approximately 11ml, and Janssen Darzalex Faspro at 15ml (1, 2). Administering this volume of drug into a patient via a syringe is an uncomfortable experience for both parties that still requires expensive HCP involvement.

Both aforementioned drug products contain a recombinant human hyaluronidase PH20 enzyme – a form of permeation enhancer that temporarily dissolves hyaluronan in the subcutaneous tissue to allow larger, more viscous fluids to flow and absorb more quickly (3). This novel technology may be of greater benefit to an autoinjector-based delivery than OBI (speed is of the essence with an autoinjector, but less so with OBI), but will also facilitate additional formulation work, resulting in volumes that are ideal for OBI. Indeed, switching activity appears to be on the rise. For example, Merck & Co's Keytruda (Pembrolizumab), one of the best-selling drugs globally and currently in IV form, is in clinical trials for SC alongside other similar 'checkpoint inhibitor' drugs (4).

It seems realistic to expect that these drugs could be delivered from an OBDS, either an OBI or ambulatory Large Volume Injector (LVI) device (e.g., worn on the belt whilst delivering through a cannula; such devices are already marketed for different purposes). The latter will probably be constrained by the drug volume, and a resultant device may move beyond what is appropriate to attach directly to the patient's body.

**Opportunities Driven by Delivery Volume**

Hence, demand is set to grow for self-administered SC delivery devices that can deliver across a range of volumes, grouped as shown (**Figure 1**).

The low volumes are well catered for by existing devices, along with larger autoinjectors advancing into the 2ml to 5ml group. This could still be a good starting point for OBI devices to establish a market position – as a differentiator from the use of one or more autoinjectors. However, even better is the next group, 5ml to 10ml, which is probably beyond the reach of autoinjectors, yet represents a realistic outcome for formulation developers working on complex, concentrated products.

Moving into the much larger volume territory, a space is opening up for LVI systems offering SC infusion, bolus delivery, and weight-based dosing, for example. Several companies have recognised this potential and have devices in development.

**Stakeholder Needs and Barriers to Entry**

As well as payers/insurers, there are three sets of stakeholders influencing this market: patients, HCPs, and pharmaceutical/biotech companies. Stakeholders' needs (and the resultant barriers to entry) can be broadly categorised into the following: ease of use, cost effectiveness, fit with existing and trusted industry processes, as well as feasibility.

***Ease of Use***

Patients and HCPs are key where ease of use is concerned, and the latter group should be recognised as a gatekeeper, or at the very least an influencer, when it comes to the adoption of devices as they reach the market. The most common need expressed regarding OBI devices is that they are prefilled and preloaded, which minimises user involvement and burden.

However, interestingly, the wearable devices on the market today do not have this configuration. Pharma companies seem to concur that this need is important; perhaps the market is waiting for a truly prefilled, preloaded, ready-to-use solution. In general, this type of device requires no user preparation or priming, which is a potential trade-off when considering an off-body LVI.

***Cost Effectiveness***

In the past, the development of sophisticated electromechanical devices may have given wearables a reputation for being high cost, significantly impacting the business case. With the likelihood that OBI devices will be single-use disposables, minimising device cost has become an important factor, balanced against the functional requirements of the device. A bolus injector could derive its expulsion mechanism from a spring or other novel means (for example: osmosis, pressure, or gas) and, if suitable user feedback solutions could be implemented, without the requirement of connectivity, motors, batteries, and electronics. This approach could lead to a more sustainable device – with further promise of reusability.

***Process-Friendly***

The pharma industry demands processes that maintain the status quo concerning primary containers, so this is a key driver. As noted, OBI devices launched, and in development, range from simple, spring-driven, piston-based systems to sophisticated electromechanical solutions, employing drug containers ranging from fill-at-point-of-use reservoirs to prefilled, standard primary containers. There is no real precedent for OBI devices yet, and there are difficult questions to answer, such as how to maintain sterility or minimise disruption to existing fill-and-finish lines.

***Feasibility***

As with any other delivery device, the capability to deliver the drug safely is of paramount importance. Given the user-loaded nature of some OBI devices, safeguarding against accidental or deliberate misuse, initiating zero risk to the drug stability, and compatibility with a host of transportation and storage requirements, must all be fully validated. From a patient perspective, it is not known if patients will accept body-worn devices or whether HCPs will support their use in certain scenarios. For example, in the oncology sector, patients are handled with extreme caution by their physicians while they are being treated with drugs with high levels of toxicity that may not ever be conducive to self-administration. That does not mean that an OBDS could never work for these products, though, as the same benefits exist in reducing HCP interaction and in-clinic time for patients who use them on-site.

For a device technology to succeed, it must prove that it can satisfy a wide range of requirements. Pharma and biotech companies are the key stakeholders with interests across the needs matrix. Historically, pharma companies may have been less interested in devices from a patient perspective, but this is no longer the case.

**Conclusion**

With a new chapter of the ISO 11608 series dedicated to OBDS published in April 2022, it is evident that the industry is taking these systems seriously (5).

A variety of generally small and discreet devices are in advanced stages of development alongside those already serving market needs. Combined with the trends described, it is clear that more OBI and LVI devices will launch. Both OBI and LVI devices are a subset of the overarching OBDS group but notionally split by volume and configuration (note: an LVI could readily be OB or ambulatory).

Such devices are distant cousins of the first 'wearable' insulin pump that was created by Dr Arnold Kadish back in the 1960s (6). While this was undoubtedly innovative at the time, it was also the size of a substantial backpack. Therefore users today must be thankful for miniaturisation!

*References*


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Prior to joining Phillips-Medisize he held project management and business development roles in the consulting industry, working on a wide range of device programmes. He now specialises in drug delivery devices.